Claims

We Claim:

1. A method for manufacturing very small particles of anticancer molecules comprising:
    a. Providing a contained space
    b. applying a solution having at least a solvent and the anticancer molecules on or close to a surface vibrating at a desired frequency within the contained space; and
    c. applying a compressed antisolvent to the contained space; and
    d. choosing the antisolvent such that it is reasonably miscible with the solvent and antisolvent does not dissolve the molecule substantially.

2. A method for manufacturing very small particles of poorly water soluble molecules comprising:
    a. Providing a contained space
    b. applying a solution having at least a solvent and the anticancer molecules on or close to a surface vibrating at a desired frequency within the contained space; and
    c. applying a compressed antisolvent to the contained space; and
    d. choosing the antisolvent such that it is reasonably miscible with the solvent and the antisolvent does not dissolve the molecule substantially.
3. The method as in claim 1 or claim 2 wherein the compressed antisolvent is near its critical point.
4. The method as in claim 1 or claim 2 wherein the compressed antisolvent is above its critical point
5. The method as in claim 1 or claim 2 wherein the compressed antisolvent is in liquid state.
6. The method as in claim 1 or claim 2 wherein the particle size can be changed by changing the amplitude of vibration
7. The method as in claim 1 or claim 2 wherein the particle size can be changed by changing the frequency of vibration
8. The method as in claim 1 or claim 2 wherein the frequency can be varied from 10 Hz to 1Ghz.
9. The method as in claim 1 or claim 2 wherein the frequency is preferably between 0.5 kHz and 0.5 Ghz.
10. The method as in claim 1 or claim 2 wherein the temperature of the contained space can be controlled
11. The method as in claim 1 or claim 2 wherein the pressure of the contained space can be controlled.
12. The method as in claim 1 or claim 2 wherein the temperature of the contained space can be varied between 0.1 times Tc and 5 times Tc
13. The method as in claim 1 or claim 2 wherein the application of solution is continuous
14. The method as in claim 1 or claim 2 wherein the application of antisolvent is continuous

15. The method as in claim 1 or claim 2 wherein the antisolvent is selected from the group consisting of ethanol, methanol, hexane, pentanes, dichloromethane, heptanes, carbon dioxide, ethane, propane, butane, sulfur hexafluoride, fluoroform, chloroform, hydrofluorocarbons, chlorofluorocarbons, isobutane, tetrahydrifuran, 1-methyl-2-pyrrolidone, dimethyl sulfoxide, dimethyl formamide, dimethyl acetamide and a combination thereof.
16. The method as in claim 1 or claim 2 wherein the antisolvent is carbon dioxide
17. The method as in claim 1 or claim 2 wherein the solvent is selected from the group consisting of ethanol, methanol, hexane, pentanes, dichloromethane, heptanes, carbon dioxide, ethane, propane, butane, sulfur hexafluoride, fluoroform, chloroform, isobutane, tetrahydrifuran, 1methyl-2-pyrrolidone, dimethyl sulfoxide, dimethyl formamide, dimethyl acetamide and a combination thereof.
18. The method as in claim 1 or claim 2 wherein the collection of the particles is continuous
19. A pharmaceutical composition comprising
    a. Particles manufactured according to claim 1 or claim 2; and
    b. At least one stabilizer.
20. An intravenous administration composition comprising
    c. Particles manufactured according to claim 1 or claim 2; and
    d. At least one stabilizer.
21. The composition as in 20 further comprising at least one isotonic liquid carrier.
22. The formulation as in claim 1 or claim 20 wherein the stabilizers are selected from the group consisting of polysorbate-80, pluronic block copolymers, lecithin, polyethylene glycol, dextran and a combination thereof.
23. The method as in claim 1 or claim 21 wherein the isotonic liquid carrier is saline or dextran.
24. The method as in claim 1 or claim 2 wherein the particles are collected inside the contained space in a liquid medium
25. The method as in claim 1 or claim 24 wherein the liquid medium is aqueous
26. The method as in claim 1 or claim 24 wherein the liquid medium is organic and substantially nonsolvent for the anticancer molecules
27. The method in claim 1 or claim 24 wherein the liquid medium is organic and has a small dissolving power for the anticancer molecules
28. The method as in claim 1 or claim 24 wherein the liquid medium is an isotonic carrier
29. The method as in claim 1 or claim 24 wherein the liquid medium contains one or more stabilizers
30. The method as in claim 1 or claim 2 wherein the contained space can withstand pressures close to 50,000 psi
31. The method as in claim 1 or claim 2 wherein the contained space can withstand temperatures close to 400 °C
32. The method as in any of the above claims wherein the produced solid particles are associated with a desired free energy.
33. The method as in any of the above claims wherein the produced particles are amorphous

34. The method as in any of the above claims wherein the produced particles are crystalline
35. The method as in any of the above claims wherein a factor selected from the group consisting of Change in temperature, Change of Solvent, Change of composition of solvents, Change of antisolvent, Change of antisolvent, Change of composition of solvents, Adding a mixing means, Changing the extend of mixing and a combination thereof result different crystal structures.

36. Methods and particles as in any one of the above claims wherein the vibration of the surface is accomplished by a piezo-electric or magneto-restrictive means
37. Particles manufactured by any of the above claims wherein the particle size range is from 0.01 nm to 50 microns
38. Particles manufactured by any of the above claims wherein the particle size range is from 0.01 nm to 0.5 microns
39. Methods and particles as in any one of the above claims wherein the anticancer molecule is poorly water soluble